

International Application No.: PCT/GB99/03302
International Filing Date: 15 October 1999
Title: "Methods of Treatment"
Filed: 13 April 2001
PRELIMINARY AMENDMENT
Express Mail Label No.: EL 709 415 018 US
Date of Deposit: 13 April 2001

46. A method according to claim 28 wherein the underlying disease is any one of AIDS, liver cirrhosis, chronic obstructive pulmonary disease with or without emphysema, chronic renal failure, chronic infections, cancer, heart disease including hypertension and chronic heart failure.

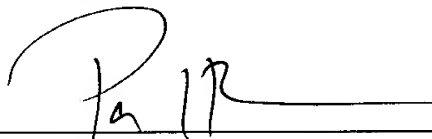
47. A method according to claim 28 wherein the patient has idiopathic cachexia.

Remarks

The claims have been amended to use proper Markush claim language and to remove multiple dependencies. No new matter has been introduced.

The attached appendices recite all claims with amendments marked and as a clean copy.

Respectfully submitted,



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APPENDIX: *Claims Marked to Show Amendments*

1. (amended) A method of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of an agent selected from the group consisting of an agent which reduces sympathetic nervous system activity and/or improves cardiovascular reflex status, a compound which inhibits the effect of aldosterone, a chymase inhibitor, a cathepsin inhibitor, a receptor blocker, an imidazoline receptor antagonist, an imidazoline receptor antagonist, a peripherally acting receptor antagonist, a ganglion blocking agent, a drug that has an effect on cardiovascular reflexes and thereby reduces SNS activity, an opiate, scopolamine, an endothelin receptor antagonist, a xanthine oxidase inhibitor, and erythropoietin.

2. A method according to Claim 1 wherein the agent which reduces sympathetic nervous system activity is any one or more of the following: a compound which inhibits the effect of aldosterone such as an aldosterone antagonist; a chymase inhibitor; a cathepsin inhibitor; a receptor blocker; an imidazoline receptor antagonist; a centrally acting receptor antagonist; a peripherally acting receptor antagonist; a ganglion blocking agent; a drug that has an effect on cardiovascular reflexes and thereby reduce SNS activity such as an opiate; scopolamine; endothelin receptor antagonist; a xanthine oxidase inhibitor; and erythropoietin.

3. (amended) A method claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a compound which inhibits the effect of aldosterone, such as an aldosterone antagonist.

4. A method according to Claim 3 wherein the compound which inhibits the effect of aldosterone is any one of spironolactone, testolactone, RU40555, RU26752, canrenoate,

eplerenone, 3-(17 -hydroxy-3-oxoandrosta-1,4,6,11-tetraen-17 -yl)propionic acid lactone, 3-(9- -fluoro-17 -hydroxy-3-oxo-androsta-4-en-17 -yl)propionic acid lactone, dihydro-spirorenone, spirorenone, 15,16-methylene derivatives of spironolactone, mespirenone and SC9420.

5. (amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a chymase inhibitor.

6. A method according to Claim 5 wherein the chymase inhibitor is any one of alendronate, aprotinin and tissue inhibitors of matrix metalloproteinases.

7. (amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a cathepsin inhibitor.

8. A method according to Claim 7 wherein the cathepsin B inhibitor is any one of an epoxysuccinyl peptide such as CA-074 or E64-c, stefin A and cystatin C.

9. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a receptor blocker.

10. A method according to Claim 9 wherein the receptor blocker is any one of acebutolol, alprenolol, atenolol, betaxolol, bisoprolol, carteolol, celiprolol, esmolol, labetolol, lavobunolol, metipranolol, metoprolol, nadolol, oxprenolol, penbutolol, pindolol, propanolol, sotalol, timolol, nebivolol, carvedilol and bucindolol.

11. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of an imidazoline receptor antagonist.

12. A method according to Claim 11 wherein the imidazoline receptor antagonist is any one of moxonidine, rilmenidine, pentamidine and -me thyl dopa.

13. (amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of an imidazoline receptor antagonist.

14. A method according to Claim 13 wherein the centrally acting receptor agonist is clonidine.

15. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a peripherally acting receptor antagonist.

16. A method according to Claim 15 wherein the peripherally acting receptor antagonist is any one of doxazosin, prazosin, terazosin and ipsapirone.

17. (amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a ganglion blocking agent.

18. A method according to Claim 17 wherein the ganglion blocking agent is any one of azamethonium, dicolinium, hexamethonium, mecamlamine, pentamethonium, pentolinium, trimetaphan, benzo hexonium, hexafluorenium, cypenam, trimethaphan canfosulfonate, tetraethylammonium bromide and synapleg.

19. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a drug that has an effect on cardiovascular reflexes and thereby reduces SNS activity.

20. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of an opiate.

21. A method according to Claim 20 wherein the opiate is any one of dihydrocodeine, morphine, diamorphine and buprenorphine.

22. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of scopolamine.

23. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of an endothelin receptor antagonist.

24. A method according to Claim 23 wherein the ET-1 receptor antagonist is any one of butenolide, BQ123, BQ-788, A-216546, ABT-627, IRL3461, LU135252, S-0139, T-0201, PD 142,893, PD 164333, RO 61-1790, PD 156,707, SB 209670, IRL 1038 and WS-7338 B.

25. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a xanthine oxidase inhibitor.

26. A method according to Claim 25 wherein the xanthine oxidase inhibitor is any one of allopurinol, 7,8-dihydroneopterin, 5,6,7,8-tetrahydrobiopterin, leukopterin, xanthopterin, neopterin, biopterin, 4-amino-6-hydroxypyrazolo[3,4-d]pyrimidine (AHPP) and oxypurinol.

27. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of erythropoietin.

28. A method of treating weight loss due to underlying disease in a patient the method comprising electrically stimulating the patient's muscles.

29. (amended) A method according to [any one of the preceding claims] claim 1 wherein the underlying disease is any one of AIDS, liver cirrhosis, chronic obstructive pulmonary disease with or without emphysema, chronic renal failure, chronic infections, cancer, heart disease including hypertension and chronic heart failure.

30. (Amended) A method according to [any one of Claims 1 to 29] claim 1 wherein the patient has idiopathic cachexia.

31. (Amended) A method according to [any one of Claims 1 to 29] claim 1 wherein the underlying disease is chronic heart failure and the patient has cardiac cachexia.

35. (Amended) A method of treating or preventing weight loss due to the [ageing] aging process in a patient the method comprising administering to the patient an effective amount of an agent which reduces sympathetic nervous system activity.

36. (Amended) A method of treating or preventing weight loss due to the [ageing] aging process in a patient the method comprising administering to the patient an effective amount of [any one or more of] a compound selected from the group consisting of a compound which inhibits the effect of aldosterone such as an aldosterone antagonist; a chymase inhibitor; a cathepsin inhibitor; a receptor blocker; an imidazoline receptor antagonist; a centrally acting receptor antagonist; a peripherally acting receptor antagonist; a ganglion blocking

agent; a drug that has an effect on cardiovascular reflexes and thereby reduce SNS activity such as an opiate, a digitalis alkaloid, scopolamine; an endothelin receptor antagonist; a xanthine oxidase inhibitor; and erythropoietin.

37. (Amended) A method of treating or preventing weight loss due to the [ageing] aging process in a patient the method comprising electrically stimulating the patient's muscles.

38. A method of enhancing exercise performance in a healthy patient the method comprising administering to the individual an effective amount of an agent which reduces sympathetic nervous system activity.

39. (amended) A method of enhancing exercise performance in a healthy individual the method comprising administering the individual an effective amount of [any one or more of] a compound selected from the group consisting of a compound which inhibits the effect of aldosterone such as an aldosterone antagonist; a chymase inhibitor; a cathepsin inhibitor; a receptor blocker; an imidazoline receptor antagonist; a centrally acting receptor antagonist; a peripherally acting receptor antagonist; a ganglion blocking agent; a drug that has an effect on cardiovascular reflexes and thereby reduce SNS activity such as an opiate; a digitalis alkaloid; scopolamine; an anabolic growth factor like growth hormone and insulin-like growth factor-I (IGF-I); an endothelin receptor antagonist; a TNF antagonist; a xanthine oxidase inhibitor; and erythropoietin.

40. A method of enhancing exercise performance in a healthy patient the method comprising electrically stimulating the patient's muscles.

41. (Amended) A method of preventing weight loss consequent to a cardiovascular disorder in a patient at risk of heart disease the method comprising administering to the

patient an effective amount of [any one or more of] a compound selected from the group consisting of a compound with an inhibiting effect on aldosterone; a α -receptor blocker; an imidazoline receptor antagonist; a centrally acting α receptoragonist; a peripherally acting receptor antagonist; and a ganglion blocking agent.

46. A method according to claim 28 wherein the underlying disease is any one of AIDS, liver cirrhosis, chronic obstructive pulmonary disease with or without emphysema, chronic renal failure, chronic infections, cancer, heart disease including hypertension and chronic heart failure.

47. A method according to claim 28 wherein the patient has idiopathic cachexia.

APPENDIX: *Clean Copy of Claims*

1. (amended) A method of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of an agent selected from the group consisting of an agent which reduces sympathetic nervous system activity and/or improves cardiovascular reflex status, a compound which inhibits the effect of aldosterone, a chymase inhibitor, a cathepsin inhibitor, a receptor blocker, an imidazoline receptor antagonist, an imidazoline receptor antagonist, a peripherally acting receptor antagonist, a ganglion blocking agent, a drug that has an effect on cardiovascular reflexes and thereby reduces SNS activity, an opiate, scopolamine, an endothelin receptor antagonist, a xanthine oxidase inhibitor, and erythropoietin.

2. A method according to Claim 1 wherein the agent which reduces sympathetic nervous system activity is any one or more of the following: a compound which inhibits the effect of aldosterone such as an aldosterone antagonist; a chymase inhibitor; a cathepsin inhibitor; a receptor blocker; an imidazoline receptor antagonist; a centrally acting receptor antagonist; a peripherally acting receptor antagonist; a ganglion blocking agent; a drug that has an effect on cardiovascular reflexes and thereby reduce SNS activity such as an opiate; scopolamine; endothelin receptor antagonist; a xanthine oxidase inhibitor; and erythropoietin.

3. (amended) A method claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a compound which inhibits the effect of aldosterone, such as an aldosterone antagonist.

4. A method according to Claim 3 wherein the compound which inhibits the effect of aldosterone is any one of spironolactone, testolactone, RU40555, RU26752, canrenoate,

eplerenone, 3-(17 -hydroxy-3-oxoandrosta-1,4,6,11-tetraen-17 -yl)propionic acid lactone, 3-(9- -fluoro-17 -hydroxy-3-oxo-androsta-4-en-17 -yl)propionic acid lactone, dihydro-spirorenone, spirorenone, 15,16-methylene derivatives of spironolactone, mespirenone and SC9420.

5. (amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a chymase inhibitor.

6. A method according to Claim 5 wherein the chymase inhibitor is any one of alendronate, aprotinin and tissue inhibitors of matrix metalloproteinases.

7. (amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a cathepsin inhibitor.

8. A method according to Claim 7 wherein the cathepsin B inhibitor is any one of an epoxysuccinyl peptide such as CA-074 or E64-c, stefin A and cystatin C.

9. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a receptor blocker.

10. A method according to Claim 9 wherein the receptor blocker is any one of acebutolol, alprenolol, atenolol, betaxolol, bisoprolol, carteolol, celiprolol, esmolol, labetolol, lavobunolol, metipranolol, metoprolol, nadolol, oxprenolol, penbutolol, pindolol, propanolol, sotalol, timolol, nebivolol, carvedilol and bucindolol.

11. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of an imidazoline receptor antagonist.

12. A method according to Claim 11 wherein the imidazoline receptor antagonist is any one of moxonidine, rilmenidine, pentamidine and -methyldopa.

13. (amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of an imidazoline receptor antagonist.

14. A method according to Claim 13 wherein the centrally acting receptoragonist is clonidine.

15. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a peripherally acting receptor antagonist.

16. A method according to Claim 15 wherein the peripherally acting receptor antagonist is any one of doxazosin, prazosin, terazosin and ipsapirone.

17. (amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a ganglion blocking agent.

18. A method according to Claim 17 wherein the ganglion blocking agent is any one of azamethonium, dicolinium, hexamethonium, mecamlamine, pentamethonium, pentolinium, trimetaphan, benzohexonium, hexafluorenium, cypenam, trimethaphan canfosulfonate, tetraethylammonium bromide and synapleg.

19. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a drug that has an effect on cardiovascular reflexes and thereby reduces SNS activity.

20. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of an opiate.

21. A method according to Claim 20 wherein the opiate is any one of dihydrocodeine, morphine, diamorphine and buprenorphine.

22. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of scopolamine.

23. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of an endothelin receptor antagonist.

24. A method according to Claim 23 wherein the ET-1 receptor antagonist is any one of butenolide, BQ123, BQ-788, A-216546, ABT-627, IRL3461, LU135252, S-0139, T-0201, PD 142,893, PD 164333, RO 61-1790, PD 156,707, SB 209670, IRL 1038 and WS-7338 B.

25. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of a xanthine oxidase inhibitor.

26. A method according to Claim 25 wherein the xanthine oxidase inhibitor is any one of allopurinol, 7,8-dihydroneopterin, 5,6,7,8-tetrahydrobiopterin, leukopterin, xanthopterin, neopterin, biopterin, 4-amino-6-hydroxypyrazolo[3,4-d]pyrimidine (AHPP) and oxypurinol.

27. (Amended) A method of claim 1 of treating weight loss due to underlying disease in a patient the method comprising administering to the patient an effective amount of erythropoietin.

28. A method of treating weight loss due to underlying disease in a patient the method comprising electrically stimulating the patient's muscles.

29. (amended) A method according to claim 1 wherein the underlying disease is any one of AIDS, liver cirrhosis, chronic obstructive pulmonary disease with or without emphysema, chronic renal failure, chronic infections, cancer, heart disease including hypertension and chronic heart failure.

30. (Amended) A method according to claim 1 wherein the patient has idiopathic cachexia.

31. (Amended) A method according to claim 1 wherein the underlying disease is chronic heart failure and the patient has cardiac cachexia.

35. (Amended) A method of treating or preventing weight loss due to the aging process in a patient the method comprising administering to the patient an effective amount of an agent which reduces sympathetic nervous system activity.

36. (Amended) A method of treating or preventing weight loss due to the aging process in a patient the method comprising administering to the patient an effective amount of a compound selected from the group consisting of a compound which inhibits the effect of aldosterone such as an aldosterone antagonist; a chymase inhibitor; a cathepsin inhibitor; a receptor blocker; an imidazoline receptor antagonist; a centrally acting receptor antagonist; a peripherally acting receptor antagonist; a ganglion blocking agent; a drug that has an

effect on cardiovascular reflexes and thereby reduce SNS activity such as an opiate, a digitalis alkaloid, scopolamine; an endothelin receptor antagonist; a xanthine oxidase inhibitor; and erythropoietin.

37. (Amended) A method of treating or preventing weight loss due to the aging process in a patient the method comprising electrically stimulating the patient's muscles.

38. A method of enhancing exercise performance in a healthy patient the method comprising administering to the individual an effective amount of an agent which reduces sympathetic nervous system activity.

39. (amended) A method of enhancing exercise performance in a healthy individual the method comprising administering the individual an effective amount of a compound selected from the group consisting of a compound which inhibits the effect of aldosterone such as an aldosterone antagonist; a chymase inhibitor; a cathepsin inhibitor; a receptor blocker; an imidazoline receptor antagonist; a centrally acting receptor antagonist; a peripherally acting receptor antagonist; a ganglion blocking agent; a drug that has an effect on cardiovascular reflexes and thereby reduce SNS activity such as an opiate; a digitalis alkaloid; scopolamine; an anabolic growth factor like growth hormone and insulin-like growth factor-I (IGF-I); an endothelin receptor antagonist; a TNF antagonist; a xanthine oxidase inhibitor; and erythropoietin.

40. A method of enhancing exercise performance in a healthy patient the method comprising electrically stimulating the patient's muscles.

41. (Amended) A method of preventing weight loss consequent to a cardiovascular disorder in a patient at risk of heart disease the method comprising administering to the

patient an effective amount of a compound selected from the group consisting of a compound with an inhibiting effect on aldosterone; a α -receptor blocker; an imidazoline receptor antagonist; a centrally acting receptoragonist; a peripherally acting receptor antagonist; and a ganglion blocking agent.

46. A method according to claim 28 wherein the underlying disease is any one of AIDS, liver cirrhosis, chronic obstructive pulmonary disease with or without emphysema, chronic renal failure, chronic infections, cancer, heart disease including hypertension and chronic heart failure.

47. A method according to claim 28 wherein the patient has idiopathic cachexia.

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JCS Rec'd PCT/PID

09/807558
13 APR 2001

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this Preliminary Amendment, and any documents referred to as attached therein, are being deposited with the United States Postal Service on this date, 13 April 2001, in an envelope as "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10, Mailing Label Number EL 709 415 018 US addressed to Box PCT, Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: April 13, 2001


Jean Hicks